

REMARKS

Upon entry of the foregoing amendment, claims 1-19 are pending for the Examiner's consideration, with claims 1 and 14 being the independent claims. Claims 18 and 19 have been withdrawn by the Examiner. Claims 1-9, 12-14, 16, and 17 are amended herein. Claim 1 has been amended to recite glucoregulatory polypeptides. Applicants respectfully submit that this amendment introduces no new matter. In this regard, the Examiner is referred, for example, to page 3, lines 16-22 of the application as originally filed. The remaining amendments are made to provide consistent antecedent basis for the claims, and introduce no new matter. Applicants respectfully submit that the present amendment, in conjunction with the following remarks, places all claims in condition for allowance, or alternatively, in better form for appeal. Accordingly, applicants respectfully request entry and consideration of the present amendment and remarks.

Rejection Under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1 and 7-13 as being anticipated by U.S. Patent No. 5,385,887 to Yim *et al.* ("the Yim patent"). Independent claim 1 has been amended herein, thereby rendering this rejection moot. Without conceding the propriety of the rejection as to the original claims, Applicants respectfully submit that this rejection cannot properly be maintained for the claims as presented herein.

Independent claim 1 has been amended herein to recite a biocompatible polylactide-co-glycolide polymer having dispersed therein a biologically active *glucoregulatory* polypeptide. The Yim patent is limited to osteogenic proteins, such as bone morphogenic proteins ("BMPs"), and provides no disclosure whatsoever regarding glucoregulatory polypeptides. For at least this reason, Applicants respectfully submit that this rejection cannot properly be maintained for the claims as presented herein.

Moreover, Applicants respectfully submit that the Examiner's reasoning regarding the "consisting essentially of" transition phrase on page 3 of the Office Action is incorrect. The Examiner asserts that "the other ingredients in Yim are merely excipients which do not fundamentally alter the structure or properties of the composition." Applicants respectfully

submit that the compositions disclosed in the Yim patent include a solubilizing agent, glutamic acid hydrochloride (HCL) being the preferred solubilizing agent. *See*, for example, column 2, lines 31-36 and column 3, lines 60-61 of the Yim patent. As discussed at column 3, lines 34-39 of the Yim patent, the solubilizing agent is needed so that a pharmaceutically effective amount of protein can be delivered without undue volumes of carrier being necessary. Therefore, Applicants respectfully submit that the solubilizing agent, *e.g.*, glutamic acid hydrochloride, materially affects a basic property of the composition, *i.e.*, release of the osteogenic protein from the composition. Accordingly, the solubilizing agent is not “merely [an] excipient[s]” as asserted by the Examiner. Therefore, the “consisting essentially of” language recited in the claims of the present application also distinguishes the claimed invention from the compositions recited in the Yim patent. For this reason as well, Applicants respectfully submit that this rejection cannot properly be maintained for the claims as presented herein.

Rejection Under 35 U.S.C. § 103(a)

The Examiner has rejected claims 2-6 and 14-17 under 35 U.S.C. § 103(a) as being unpatentable over the Yim patent in view of U.S. Patent No. 6,506,724 to Hiles *et al.* (“the Hiles patent”). Applicants respectfully submit that the Examiner has not established a *prima facie* case of obviousness because there is no motivation to combine the Yim and Hiles patents in the manner suggested by the Examiner, and, even if the documents are combined, the claimed invention does not result.

As recognized by the Examiner, the Yim patent provides no teaching whatsoever regarding the use of exendin-4, or other glucoregulatory polypeptides. The Examiner attempts to cure this deficiency in the Yim patent by citing to the Hiles patent, which discloses the use of exendins for the treatment of diabetes. The sole motivation noted by the Examiner for combining the documents is the treatment of diabetes using exendin-4. However, as relied upon by the Examiner in withdrawing claims 18-19 directed to methods of treating, claims 2-6 and 14-17 are limited to the composition itself. There is no disclosure in the Yim patent that would motivate one skilled in the art to replace an osteogenic protein with a glucoregulatory polypeptide such as exendin-4 in the compositions disclosed in the Yim patent. Similarly, there is no disclosure in the Hiles patent that would motivate one skilled in the art to incorporate

exendin-4 in a biocompatible polymer with a sugar and glycine. Simply put, contrary to the Examiner's assertion, there is no motivation or suggestion to combine the teachings of the Yim and Hiles patents to make a composition as claimed. For at least this reason, Applicants respectfully submit that this rejection cannot properly be maintained.

Even if the Yim and Hiles patents could be properly combined, which Applicants do not concede, the invention as claimed does not result. As discussed above, the composition disclosed in the Yim patent includes a solubilizing agent, such as glutamic acid hydrochloride, that ensures that a pharmaceutically effective amount of the protein can be delivered. Such a solubilizing agent is excluded from the invention as claimed by the "consisting essentially of" transitional language. Therefore, even if the composition disclosed in the Yim patent could be modified to replace the osteogenic protein with exendin-4, the claimed invention does not result because the composition would include a solubilizing agent, and, therefore, would not consist essentially of exendin-4, a sugar, and glycine as claimed. For at least this reason as well, Applicants respectfully submit that this rejection cannot properly be maintained.

It would be impermissible to modify the compositions disclosed in the Yim patent to remove the solubilizing agent because that would change the principle of operation of the compositions disclosed in the Yim patent. In particular, in the compositions of the Yim patent, the solubilizing agent ensures that a pharmaceutically effective amount of the protein can be delivered. As such, modifying the compositions of the Yim patent to remove the solubilizing agent would alter the mechanism of delivery of the protein from the compositions. If a proposed modification would change the principle of operation of the prior art invention being modified, then the teachings of the reference are not sufficient to render the claims *prima facie* obvious. M.P.E.P. § 2143.01 VI. For this reason as well, Applicants respectfully submit that this rejection cannot properly be maintained.

CONCLUSION

Applicants respectfully submit that the foregoing remarks demonstrate that entry of these amendments places the present application in condition for allowance, or alternatively, in better form for consideration on appeal. All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore

respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to pass this application to issue.

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Respectfully submitted,

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